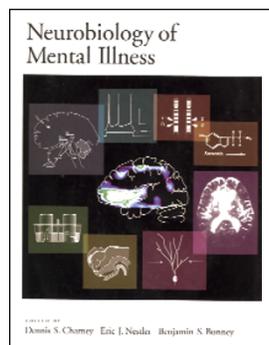


# The two revolutions



## *Neurobiology of Mental Illness*

edited by D.S. Charney, E.J. Nestler and B.S. Bunney

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*Reviewed by Trevor Robbins*

This 70-chapter edited volume of about a thousand pages is a landmark publication in psychiatry and neuroscience, and will be a compelling yardstick of progress in psychiatry for years to come. It appears at a crucial time, when documentation of the genome of humans and other animals has begun to reveal the potential of psychiatric genetics. However, this volume's main inspiration, as the editors and contributors acknowledge, has been the rise of neuroscience: the understanding of neurotransmission and drug action, and, more recently, the progress of neuroimaging techniques. The causes of mental illness can rarely be defined as distinct brain abnormalities, although few would dispute the association of psychopathology with brain malfunction. Therefore, we must consider more subtle changes in neuroendocrine balance and neuromodulation, abnormal development within specific neuronal circuitries, and dynamic aberrations in communication between structures with complex cognitive functions. This book provides an exhaustive but exhilarating compilation of such information, while wisely providing the clinician with general principles to make sense of it all. The basic neuroscientist will be inspired by studying human psychopathology, which many of us spend years trying to capture in the laboratory, and from which we (often naively) seek justification to support our research.

I suspect, however, that the revolution in psychiatry promised from the giant strides in neurobiology and genetics will be hampered by our relative slowness to latch onto another, quieter revolution: what I hope will be an increasing emphasis on behavior and cognition in biological psy-

chiatry. Not to detract from the advances in psychiatric nosology that are so well documented in this volume, but the DSM-IV (the Diagnostic and Statistical Manual of the American Psychiatric Association) is a classificatory system, not a theory. It may be useful to catalog and systematize the descriptions of a bewildering array of bizarre symptoms. However, even given the sophistication of DSM-IV, similar categorizations can sometimes result from contrasting symptomatology, and the resulting heterogeneity can be lethal to scientific advance. More theory (or in the infernal jargon term, 'construct validation') is needed to close the loop between normal and abnormal brain function in terms of their mediation of well-defined normal behavioral and physiological processes, and to make sense of phenomenology. For example, what underlying mechanisms of depression at a cognitive or behavioral level map onto cingulate and frontal cortex abnormalities? Is depression caused by a fundamental deficiency in the processing of 'reward' (whatever that is) or punishment or both? What is the role of attribution, not only in depression and psychotic delusions, but also in drug abuse? How do different forms of learning contribute to the manifestations of anxiety? What are personality traits? How do the effects of psychoactive drugs depend on behavioral and experiential context?

As this book makes abundantly clear, psychiatric disorders are often related to many genes, each having small effects, with epistatic interactions of such complexity that we can only begin to conceive of their impact. These interactions presumably lead to distributed, multivariate changes in sometimes unrelated neural systems, which are modulated by environmental and neurodevelopmental variables. In addition, the brain's output, in terms of behavior in response to environmental demands, itself powerfully determines gene expression, so

the traditional reductionist agenda is exposed as too simplistic. Overall, if neuropsychiatry is to progress further, knowledge of genotype and neurobiological and DSM-IV phenotypes must be augmented by comparable specification of behavioral and cognitive phenotypes.

The editors hope that they "will share in our excitement over the tremendous opportunities now available in behavioral neuroscience," and certainly existing advances are mentioned by some of their contributors, mainly from critical perspectives (of varying cogency) of 'animal models.' However, there is a relative dearth of information, instruction and discussion of matters like the analysis of symptom clusters by multivariate statistics, the cognitive effects of drugs such as benzodiazepines and serotonergic agents, and the proper measurement of such constructs as impulsivity and attention. I could not find any discussion of the evidence that early indications of Alzheimer's disease are dominated by deficits in episodic memory. For localizing brain abnormality, neuropsychological methods sometimes seem to be considered less important than imaging techniques, but this misses the point. In any case, the strength of functional brain imaging, on which neuropsychiatry in particular must depend, is determined by the ingenuity, as well as the theoretical relevance of the cognitive tasks used.

Of course, this reflects in part my own bias, and the contributors will justly point to space limitations that prevented them from adequately grappling with this other (hopefully not entirely parallel) universe. However, a heroic author, W.A. Lishman, attempting to cover some similar (but not identical) ground in *Organic Psychiatry*<sup>1</sup>, another book of about a thousand pages, found space to discuss psychological and cognitive aspects in more depth, albeit from a clinical perspective. His treatment of the neurobiological aspects of mental illness, while critical, was necessarily less detailed than the present encyclopedic work. Indeed, it is fascinating to compare the different approaches (and cultures) represented by these two remarkable books.

Overall, the editors of *The Neurobiology of Mental Illness* should be congratulated. The book's daunting size belies my enjoyment in reading many of the chapters; I also appreciated the modesty of the editors' suggestion that the book was a "progress report" on some of the most challenging problems in neuroscience. I await the next report with great anticipation.

1. Lishman, W. A. *Organic Psychiatry* 3rd edn. (Blackwell Science, Oxford, 1998).

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